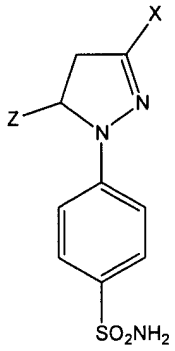
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Previously presented) A compound of the formula I:



(I)

wherein:

X is trihalomethyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

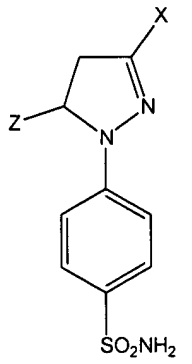
2. (Original) A compound according to claim 1 wherein Z is selected from the group consisting of substituted and unsubstituted heteroaryl; or a pharmaceutically acceptable salt thereof.

3. (Currently amended) A compound according to claim 2 wherein [[Z]] said heteroaryl is selected from the group consisting of ~~substituted and unsubstituted~~ indolyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, imidazolyl, pyrazolyl, thiazolyl, benzothiazolyl, quinolinyl, and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

4. (Original) A compound according to claim 1 wherein Z is 3-indolyl; or a pharmaceutically acceptable salt thereof.

5. (Original) A compound according to claim 1 wherein X is trifluoromethyl.

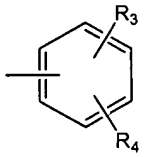
6. (Currently amended) A compound of the formula I:



(I)

wherein:

X is a group of formula II:



(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl which is mono-substituted with hydroxyl, nitro, carboxy, C_1-C_6 trihaloalkyl or cyano; phenyl which is di-substituted; and phenyl which is tri-substituted;

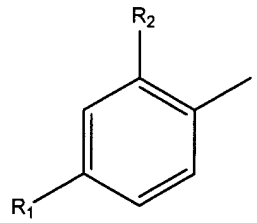
provided when Z is substituted or unsubstituted heteroaryl, it is selected from the group consisting of ~~substituted and unsubstituted~~ pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl);

or a pharmaceutically acceptable salt thereof.

7. (Currently amended) A compound according to claim 6 wherein Z is selected from the group consisting of phenyl mono-substituted with hydroxyl, nitro, carboxy, C_1-C_6 trihaloalkyl or cyano, [[di-]] di-substituted phenyl and tri-substituted phenyl.

8. (Cancelled)

9. (Currently amended) A compound according to claim 6 wherein Z is the group:



(III)

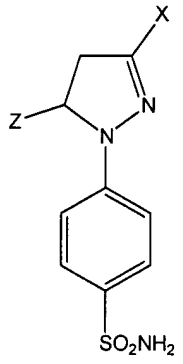
wherein R_1 and R_2 are independently selected from the group consisting of fluorine, bromine, chlorine, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxyl and nitro; or a pharmaceutically acceptable salt thereof.

10. (Currently amended) A compound according to claim 6 wherein Z is substituted or unsubstituted heteroaryl, wherein said heteroaryl is indolyl, furyl, pyridyl or benzofuryl; or a pharmaceutically acceptable salt thereof.

11. (Original) A compound according to claim 10 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

12. (Original) The compound according to claim 1 which is 1-(4-sulfamylphenyl)-3-trifluoromethyl-5-(3-indolyl)-2-pyrazoline; or a pharmaceutically acceptable salt thereof.

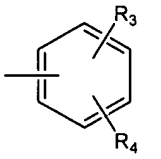
13. (Currently amended) A compound of the formula I:



(I)

wherein:

X is a group of formula II:



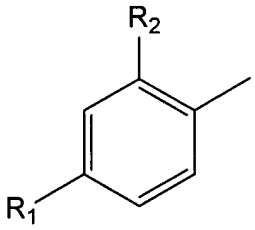
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of ~~hydrogen,~~ C_1-C_6 alkyl and C_1-C_6 alkoxy;

Z is selected from the group consisting of phenyl monosubstituted with hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the group consisting of ~~substituted and unsubstituted~~ pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

14. (Currently amended) A compound according to claim 13 wherein Z is the group:

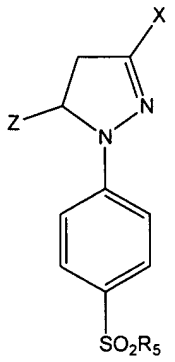


wherein R_1 and R_2 are independently selected from the group consisting of fluorine, bromine, chlorine, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxyl and nitro; or a pharmaceutically acceptable salt thereof.

15. (Currently amended) A compound according to claim 13 wherein Z is substituted or unsubstituted heteroaryl, wherein said heteroaryl is indolyl, furyl, pyridyl or benzofuryl; or a pharmaceutically acceptable salt thereof.

16. (Original) A compound according to claim 15 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

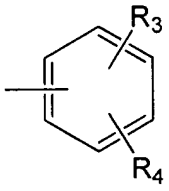
17. (Currently amended) A compound of the formula V:



(V)

wherein:

X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl, and a group of formula II:



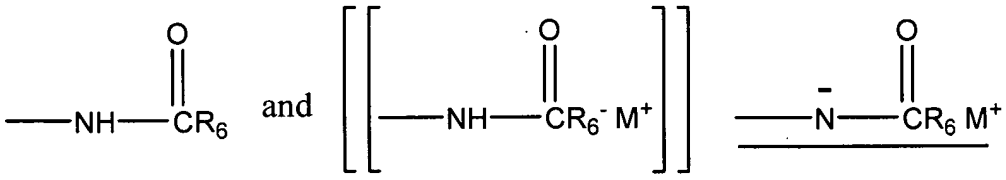
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

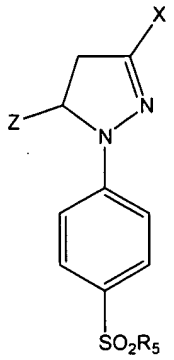
Z is substituted or unsubstituted heteroaryl; and

R_5 is selected from the group consisting of:



wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof.

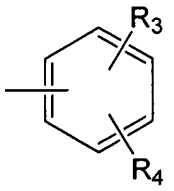
18. (Currently amended) A compound of the formula V:



(V)

wherein:

X is a group of formula II:



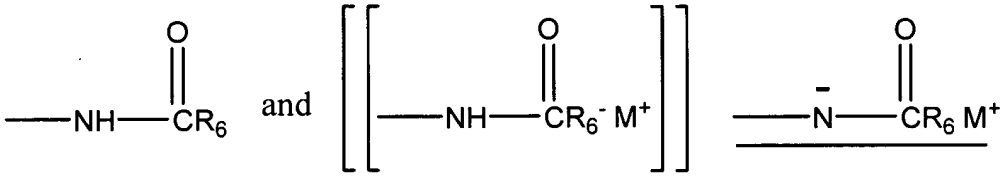
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6, alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl; and

R_5 is selected from the group consisting of:



wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li or a pharmaceutically acceptable salt thereof.

19. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

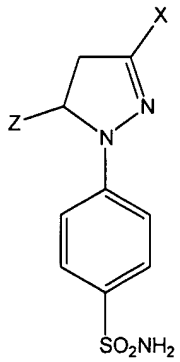
20. (Original) A method for treating a cyclooxygenase-mediated disorder comprising administering to a patient in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

21. (Original) A method for treating inflammation or an inflammation-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

22. (Original) A method for treating a neoplasia comprising administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

23. (Original) A method for treating an angiogenesis-mediated disorder administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

24. (Currently amended) A method for producing a compound of formula I:



(I)

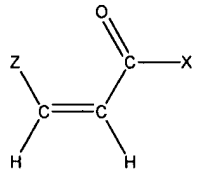
wherein:

the group X is trihalomethyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl, other than substituted and unsubstituted phenyl;

the method comprising:

(a) reacting a compound of the formula IV:



(IV)

wherein X and Z are so defined;

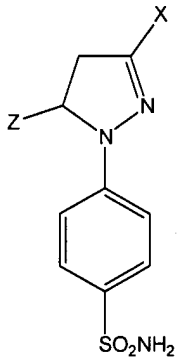
with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

25. (Original) A method according to claim 24 wherein Z is substituted or unsubstituted heteroaryl.

26. (Original) A method according to claim 24 wherein X is a radical of formula II.

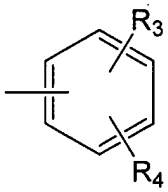
27. (Currently amended) A method for producing a compound of formula I:



(I)

wherein:

the group X is a radical of formula II:



(II)

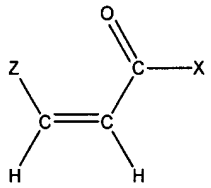
wherein:

~~wherein~~ R_3 and R_4 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C_1-C_6 alkyl, C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl which is mono-substituted with hydroxyl, nitro, carboxy; C_1-C_6 trihaloalkyl or cyano; phenyl which is di-substituted, and phenyl which is tri-substituted;

the method comprising:

(a) reacting a compound of the formula IV:



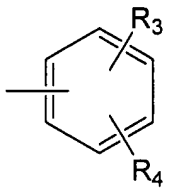
(IV)

wherein X and Z are so defined;

with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

28. (Currently amended) A method according to claim 27 wherein the group X in the reactant compound of formula IV is a radical of formula II:



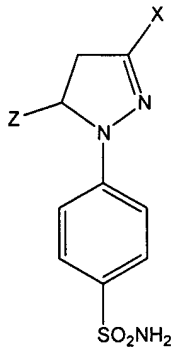
(II)

wherein:

~~wherein~~ R_3 and R_4 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C_1-C_6 alkyl, C_1-C_6 alkoxy; and carboxy.

29. (Original) An isolated optical isomer of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

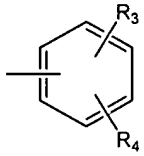
30. (Previously presented) An isolated optical isomer of a compound of the formula I:



(I)

wherein:

X is a group of formula II:



(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl;

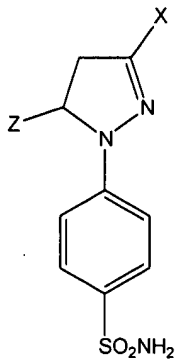
or a pharmaceutically acceptable salt thereof.

31. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 1.

32. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 6.

33. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 13.

34. (Previously presented) A method for treating a cyclooxygenase-mediated disorder comprising administering to a patient in need of such treatment an effective amount of a compound according to formula I:



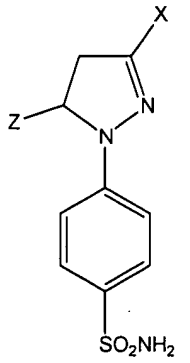
(I)

wherein:

X is selected from the group consisting of trihalomethyl and C_1-C_6 alkyl;

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

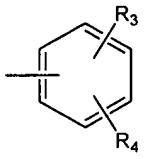
35. (Currently amended) A method for treating a cyclooxygenase-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to formula I:



(I)

wherein:

X is a group of formula II:



(II)

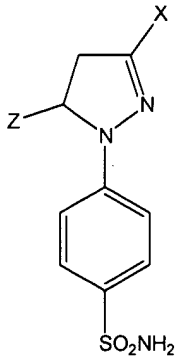
wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl, and substituted and unsubstituted heteroaryl;

~~when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted~~ wherein said heteroaryl is selected from the group consisting of pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

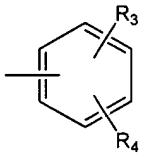
36. (Currently amended) A method for treating a cyclooxygenase-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to formula I:



(I)

wherein:

X is a group of formula II:



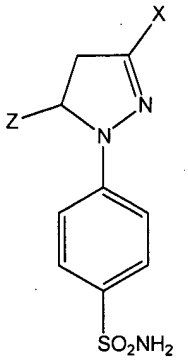
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of ~~hydrogen,~~ C_1-C_6 alkyl and C_1-C_6 alkoxy;

Z is selected from the group consisting of phenyl; phenyl monosubstituted with halogen, hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and ~~heteroaryl~~ substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the group consisting of ~~substituted and unsubstituted~~ pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

37. (Previously presented) A method for treating inflammation or an inflammation-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to formula I:



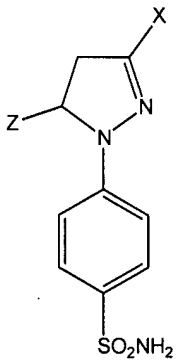
(I)

wherein:

X is selected from the group consisting of trihalomethyl and C_1-C_6 alkyl;

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

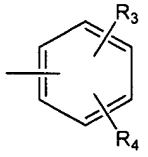
38. (Currently amended) A method for treating inflammation or an inflammation-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to formula I:



(I)

wherein:

X is a group of formula II:



(II)

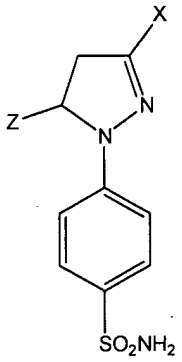
wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl, and substituted and unsubstituted heteroaryl;

~~when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted~~ wherein said heteroaryl is selected from the group consisting of pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

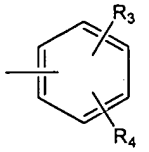
39. (Currently amended) A method for treating inflammation or an inflammation-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to formula I:



(I)

wherein:

X is a group of formula II:



(II)

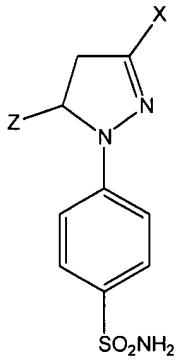
wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and C_1-C_6 alkoxy;

Z is selected from the group consisting of phenyl; phenyl monosubstituted with halogen, hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the

group consisting of ~~heteroaryl selected from the group consisting of substituted and unsubstituted~~ pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

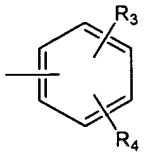
40. (Currently amended) A method for treating a neoplasia that expresses a cyclooxygenase, comprising administering to a subject in need of such treatment an effective amount of a compound of the formula I



(I)

wherein:

X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl, and a group of formula II:



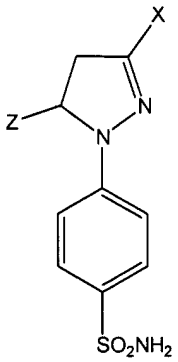
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl, mono- or di-substituted with hydroxyl, nitro, or carboxy; and tri-substituted phenyl; or a pharmaceutically acceptable salt thereof.

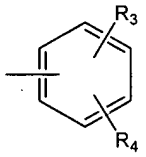
41. (Original) A method for treating an angiogenesis-mediated disorder administering to a subject in need of such treatment an effective amount of a compound of the formula:



(I)

wherein:

X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl, and a group of formula II:



(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl; or a pharmaceutically acceptable salt thereof.

42. (Original) A method according to claim 40 or 41 wherein Z is selected from the group consisting of substituted and unsubstituted heteroaryl; or a pharmaceutically acceptable salt thereof.

43. (Currently amended) A method according to claim 42 wherein [[Z]] <u>said heteroaryl</u> is selected from the group consisting of substituted and unsubstituted indolyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, imidazolyl, pyrazolyl, thiazolyl,

benzothiazolyl, quinolinyl, and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

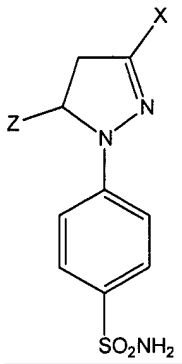
44. (Original) A method according to claim 43 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

45. (Original) A method according to claim 40 or 41 wherein X is trifluoromethyl.

46. (Original) A method according to claim 40 or 41 wherein X is a group according to formula II wherein R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1 -C_6 trihaloalkyl; and cyano; or a pharmaceutically acceptable salt thereof.

47. (Original) A method according to claim 46 wherein Z is selected from the group consisting of unsubstituted phenyl; and mono-, di- and tri-substituted phenyl.

48. (New) A compound of the formula I:



(I)

wherein:

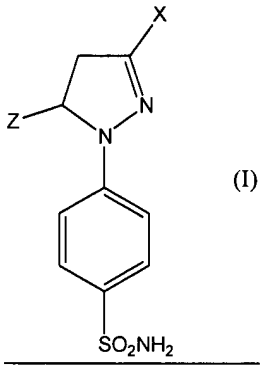
X is C_1-C_6 alkyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl;

provided when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, indolyl, benzothienyl, benzofuryl, imidazolyl,

pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

49. (New) A method for producing a compound of formula I:



(I)

wherein:

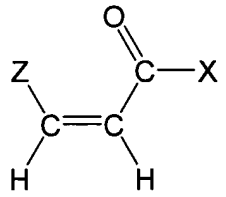
the group X is C_1-C_6 alkyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl, other than substituted and unsubstituted phenyl;

provided when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl);

the method comprising:

(a) reacting a compound of the formula IV:



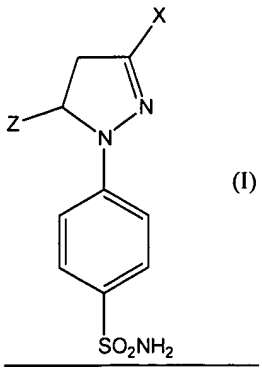
(IV)

wherein X and Z are so defined;

with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

50. (New) An isolated optical isomer of a compound of the formula I:



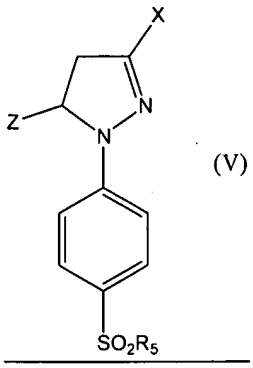
(I)

wherein:

X is selected from the group consisting of trihalomethyl and C_1-C_6 alkyl;

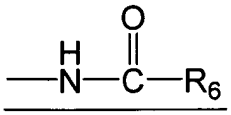
Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl that is mono-substituted or di-substituted with substituents independently selected from the group consisting of hydroxyl, nitro, and carboxy; and phenyl that is tri-substituted; or a pharmaceutically acceptable salt thereof.

51. (New) A method for producing a compound of formula V:



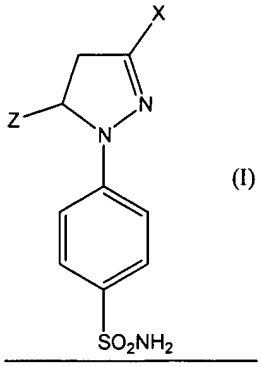
(V)

wherein R_5 is:



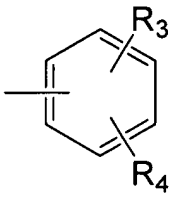
wherein R_6 is C_1-C_6 alkyl; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(I)

wherein X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl and a group of the formula II:



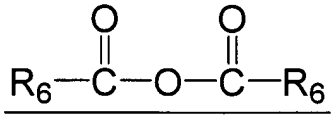
(II)

wherein:

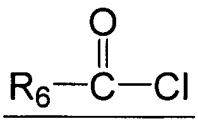
R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted heteroaryl;

with an anhydride of the formula:



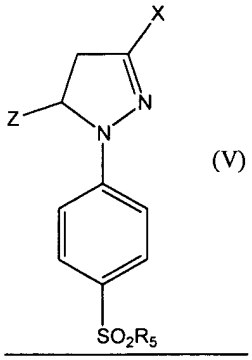
or an acylating compound of the formula:



wherein R_6 is C_1-C_6 alkyl; and

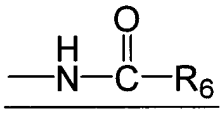
(b) isolating a compound according to formula V from the reaction products.

52. (New) A method for producing a compound of formula V:



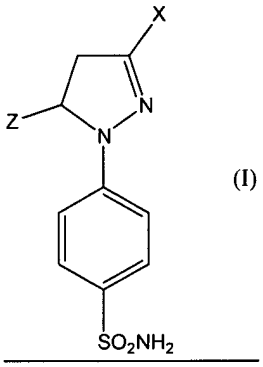
(V)

wherein R_5 is:



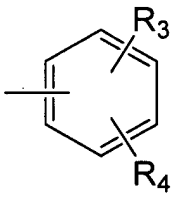
wherein R_6 is C_1-C_6 alkyl; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(I)

wherein X is a group of the formula II:

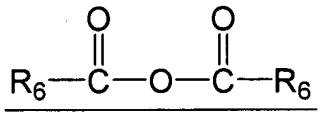


(II)

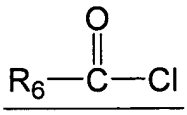
wherein: R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted aryl;

with an anhydride of the formula:



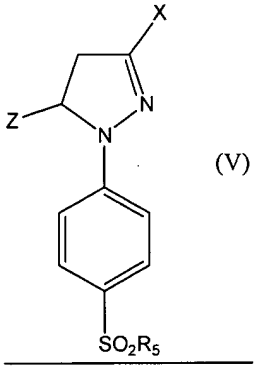
or an acylating compound of the formula:



wherein R_6 is C_1-C_6 alkyl; and

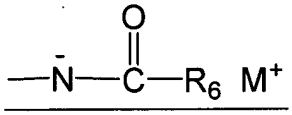
(b) isolating a compound according to formula V from the reaction products.

53. (New) A method for producing a compound of formula V:



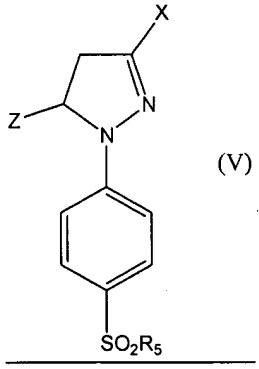
(V)

wherein R_5 is:



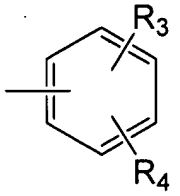
wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(V)

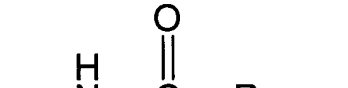
wherein X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl and a group of the formula II:



(II)

wherein: R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted heteroaryl; and

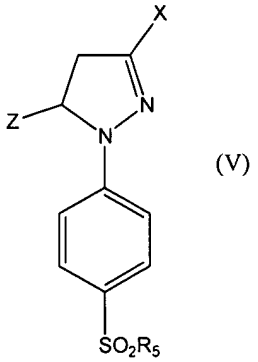
R_5 is  ; and

wherein R_6 is as defined above,

with an alkali hydroxide selected from the group consisting of NaOH, KOH and LiOH; and

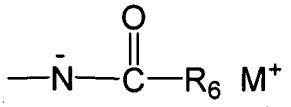
(b) isolating a compound according to formula V from the reaction products.

54. (New) A method for producing a compound of formula V:



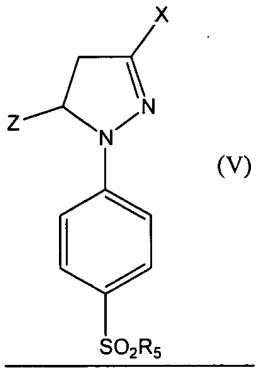
(V)

wherein R_5 is:



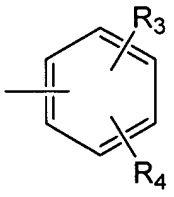
wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(V)

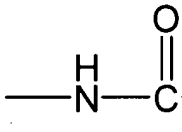
wherein X is a group of the formula II:



(II)

wherein: R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted aryl; and

R_5 is  ; and

wherein R_6 is as defined above,

with an alkali hydroxide selected from the group consisting of NaOH, KOH and LiOH; and

(b) isolating a compound according to formula V from the reaction products.